

Acute renal failure associated with a labetalol overdose

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Summary: A case of acute renal failure in association with a deliberate labetalol overdose is described. The possible pathogenetic mechanisms behind the deterioration in renal function are discussed. Treatment of β -blockade overdose, with special emphasis on the place of glucagon in such poisoning, is reviewed.

Introduction

Overdosing with beta-adrenergic blocking agents may lead to severe haemodynamic compromise and even patient death.^{1,2} Prolonged and severe hypotension, often in previously hypertensive patients, is common. However acute renal failure following an overdose with pure beta-blockers has been reported only once in a setting of complicated rhabdomyolysis.³ In addition, a reduction in the severity of experimental acute renal failure by using beta-blockers has been described.⁴

Labetalol, a non-selective β -blocker and a selective α_1 -antagonist, has caused acute renal failure in at least one patient.⁵ We hereby describe a second such case and discuss the possible pathogenic mechanisms involved together with therapy of such a potentially dangerous overdose.

Case report

A 25 year old male, previously healthy, was admitted 3 hours after self-ingestion of 6 grams of labetalol (thirty 200 mg tablets) and 7 pints of lager. The labetalol tablets had been prescribed for the patient's father for hypertension. On initial examination the patient was responsive but drowsy, with a blood pressure of 40-65/25 mmHg and pulse rate 72 regular/min. Respiration was slightly irregular and neurological examination normal. Oxygenation was adequate, but acidosis and a serum creatinine of 128 μ mol/l were noted. An electrocardiogram showed normal sinus rhythm. A toxicology screen excluded salicylate or paracetamol overdosage. Initial therapy included atropine, isoprenaline and dobutamine but hypotension proved resistant to this therapy. Oligo-anuria developed within 3 hours of admission

(urine output: 4–5 cc/hour). On the afternoon of the first day of admission (15 hours after ingestion) glucagon therapy was started, using an intravenous bolus of 10 mg, and thereafter maintained at an infusion rate of 4 mg/h. Isoprenaline was continued. Within 6 hours blood pressure had risen to 120/60 mmHg. However oligo-anuria persisted; serum urea had risen to 13.7 mmol/l and serum creatinine had risen to 354 μ mol/l. Creatine phosphokinase levels were normal. By the second day the patient was fully conscious and normotensive and inotropic therapy was gradually withdrawn. On the 3rd day of admission the patient was transferred to the renal unit with severe renal failure (serum urea: 32.6 mmol/l, serum creatinine: 806 μ mol/l). An abdominal ultrasound revealed a right kidney 12.1 cm in length and a left kidney 12.7 cm in length. No hydronephrosis was seen. Haemodialysis was commenced using a double-lumen subclavian vein catheter. The patient remained dialysis-dependent for 16 days. A spontaneous diuresis was noted on the 15th day post-overdose, and by the 30th day serum creatinine had reached a nadir of 85 μ mol/l. Recent onset hypertension is now adequately controlled with nifedipine 20 mg twice daily.

Discussion

Labetalol has a dual action as both a selective α_1 -antagonist and a non-selective β -blocker. It is used in the treatment of all forms of hypertension.⁶ Adverse side effects are minimal, but can include postural hypotension, dizziness, fatigue and less commonly depression, impotence and fever.^{7–9} Overdosage with labetalol is rare but acute renal failure with such an overdose has occurred.⁵

In 1984, Weinstein reviewed poisoning with β -blocking agents. He found no reports of acute renal failure and this despite the profound and long-lasting hypotension that often accompanies

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β -blockage overdosage.² With this severe hypotension, autoregulation in the kidney is arguably lost and further dilatation of the preglomerular afferent arteriole does not take place.¹⁰ In such a setting both renal plasma flow and glomerular filtration rate would be expected to fall. However, the massive β -blockade produces an uninterrupted stimulation to α -adrenergic receptors. This results in a post-glomerular efferent arteriole vasoconstriction, an increase in intraglomerular pressures and a possible maintenance of glomerular filtration rate. On the other hand, labetalol overdoses will have much the same characteristics of β -blockade, but its selective α_1 receptor antagonism will also lead to an efferent arteriole vasodilatation, a fall in intraglomerular pressure and a sharp reduction in renal function. Such a haemodynamic mechanism has been postulated for acute renal failure¹¹ and can be regarded as analogous to the acute renal failure seen when angiotensin converting enzyme inhibitors are given to patients with renal artery stenosis.¹²

There can be no doubt that labetalol was instrumental in causing an oliguric acute renal failure in this patient. The patient had been healthy prior to

the overdose with a serum creatinine of 128 $\mu\text{mol/l}$ on admission and became rapidly oligo-anuric and dialysis-dependent over 16 days following labetalol poisoning. Furthermore, no adverse interaction between labetalol and alcohol has been reported. Acute tubular necrosis is the most probable histological diagnosis, but as a spontaneous diuresis and recovery of renal function occurred, renal biopsy was not performed.

Early, intensive efforts must be made to correct the hypotension associated with labetalol overdose. It may be that the drug of choice is glucagon and not only a combination of β -agonists and atropine. In 1984 glucagon was the only treatment that consistently produced an increase in both blood pressure and heart rate when used to combat β -blocker overdose. All cases treated with glucagon have had a favourable outcome.² Glucagon has also helped reverse hypotension secondary to anaphylactoid shock in a patient treated previously with a β -blocker.¹³ It is felt that glucagon has potent inotropic and chronotropic actions, whose adrenergic effects are minimally antagonized by β -blockers.

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